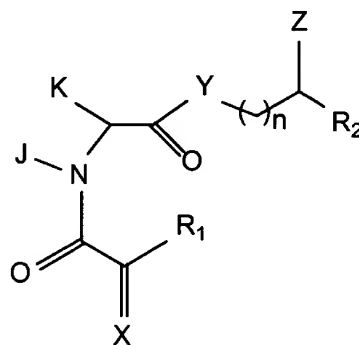




We claim:

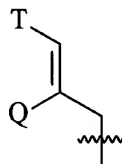
1. A method of treating a neurological activity in an animal, comprising:  
administering to said animal an effective amount of a compound having an  
affinity for FKBP-type immunophilins according to formula I



Formula I

or a pharmaceutically acceptable salt thereof,

- wherein Y is CH<sub>2</sub>, O, NH, or N-(C1-C4 alkyl);
- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns, or



- wherein Q is hydrogen, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl;
- wherein T is Ar or substituted 5-7 membered cycloalkyl with substituents at positions 3 and 4 which are independently selected from the group consisting of hydrogen, hydroxyl, O-(C1-C4)-alkyl or O-(C1-C4)-alkenyl and carbonyl;
- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, 1,2-methylenedioxy, carbonyl and phenyl;
- wherein R<sub>1</sub> is either hydrogen or U; X is either oxygen or CH-U, provided that if R<sub>1</sub> is hydrogen, then X is CH-U, or if X is oxygen then R<sub>1</sub> is U;
- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar (Ar as described above);
- wherein J is hydrogen or C1 or C2 alkyl or benzyl; K is (C1-C4)-straight or branched alkyl, benzyl or cyclohexylethyl; or wherein J and K may be taken

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together to form a 5-7 membered heterocyclic ring which may contain an oxygen (O), sulfur (S), SO or SO<sub>2</sub> substituted therein;

D1

- wherein n is 0-3; and

- wherein said neurological activity does not include amyotrophic lateral sclerosis.

2. The method of claim 1, wherein the neurological activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.

3. The method of claim 2, wherein the neurological disorder is selected from the group consisting of peripheral neuropathies cause by physical injury or disease state, physical damage to the brain, physical damage to the spinal cord, stroke associated with brain damage, and neurological disorders relating to neurodegeneration.

4. The method of claim 3, wherein the neurological disorder is Alzheimer's Disease or Parkinson's Disease.

5. The method of claim 1, wherein J and K are taken together to form a 5 membered heterocyclic ring.

6. The method of claim 5,

- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-

D2

straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and

- wherein Ar is selected from the group consisting monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

7. The method of claim 6, wherein

- if X is O, Y is O, NH or N-(C1-C4 alkyl), R<sub>1</sub> is C1-C6 straight or branched alkyl, C2-C6 straight or branched alkenyl, C5-C7 cycloalkyl or cycloalkenyl substituted with C1-C4 straight or branched alkyl or C2-C4 straight or branched alkenyl, and Ar is 1-naphthyl, 2-naphthyl, indolyl, 2-furyl, 3-furyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl

- then (CH<sub>2</sub>)<sub>n</sub>Z and R<sub>2</sub> taken together do not form:

1) substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl

2) an alkyl or alkenyl chain with substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl

3) an alkyl or alkenyl chain substituted with C5-C7 cycloalkyl.

8. The method of claim 1, wherein J and K are taken together to form a 6 membered heterocyclic ring.

9. The method of claim 8,

- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and
- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

10. The method of claim 9, wherein
  - if n is 0, X is O, Y is O, R<sub>1</sub> is 1,1-dimethyl-1-propyl, and R<sub>2</sub> is 2-phenylethyl, then Z is not 1,1-dimethyl-1-prop-2-enyl, phenyl, cyclohexyl, or 3-(N,N-diallyl)benzamide; and
  - if n is 0, X is O, Y is O, R<sub>1</sub> is tert-butyl, and R<sub>2</sub> is 2-(3',4',5'-trimethoxyphenyl)ethyl, then Z is not phenyl.
11. The method according to claim 1, further comprising co-administering to said

animal an effective amount of a neurotrophic factor selected from the group consisting of nerve growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, and neurotrophin-3.

12. The method of claim 11, wherein the neurological activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration and treatment of a neurological disorder.

13. The method of claim 12, wherein the neurological disorder is selected from the group consisting of peripheral neuropathies caused by physical injury or disease state, physical damage to the brain, physical damage to the spinal cord, and neurological disorders relating to neurodegeneration.

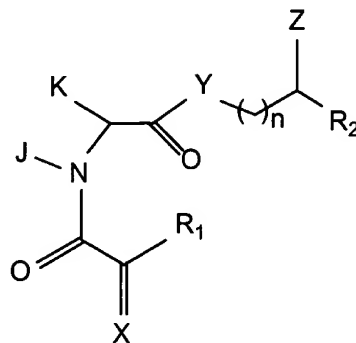
14. The method of claim 12, wherein the neurological disorder is Alzheimer's Disease or Parkinson's Disease.

15. The method of claim 11, wherein J and K are taken together to form a 5 membered heterocyclic ring.

16. The method of claim 11, wherein J and K are taken together to form a 6 membered heterocyclic ring.

17. A method for preventing neurodegeneration in an animal, comprising:

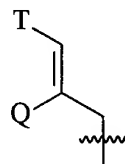
administering to said animal an effective amount of a compound having an affinity for FKBP-type immunophilins according to formula I



Formula I

or a pharmaceutically acceptable salt thereof,

- wherein Y is CH<sub>2</sub>, O, NH, or N-(C1-C4 alkyl);
- wherein X and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns, or



- wherein Q is hydrogen, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl;



- wherein T is Ar or substituted 5-7 membered cycloalkyl with substituents at positions 3 and 4 which are independently selected from the group consisting of hydrogen, hydroxyl, O-(C1-C4)-alkyl or O-(C1-C4)-alkenyl and carbonyl;
- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, 1,2-methylenedioxy, carbonyl and phenyl;
- wherein R<sub>1</sub> is either hydrogen or U; X is either oxygen or CH-U, provided that if R<sub>1</sub> is hydrogen, then X is CH-U, or if X is oxygen then R<sub>1</sub> is U;
- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar (Ar as described above);
- wherein J is hydrogen or C1 or C2 alkyl or benzyl; K is (C1-C4)-straight or branched alkyl, benzyl or cyclohexylethyl; or wherein J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain an oxygen (O), sulfur (S), SO or SO<sub>2</sub> substituted therein;

- wherein n is 0-3; and
- wherein the neuronal degeneration is not caused by amyotrophic lateral sclerosis.

18. The method of claim 17, wherein J and K are taken together to form a 5 membered heterocyclic ring.

19. The method of claim 18,

- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;
- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and
- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently

selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

20. The method of claim 19, wherein

- if X is O, Y is O, NH or N-(C1-C4 alkyl), R<sub>1</sub> is C1-C6 straight or branched alkyl, C2-C6 straight or branched alkenyl, C5-C7 cycloalkyl or cycloalkenyl substituted with C1-C4 straight or branched alkyl or C2-C4 straight or branched alkenyl, and Ar is 1-naphthyl, 2-naphthyl, indolyl, 2-furyl, 3-furyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl

- then (CH<sub>2</sub>)<sub>n</sub>Z and R<sub>2</sub> taken together do not form:

- 1) substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl
- 2) an alkyl or alkenyl chain with substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl
- 3) an alkyl or alkenyl chain substituted with C5-C7 cycloalkyl.

21. The method of claim 17, wherein J and K are taken together to form a 6 membered heterocyclic ring.

- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and

- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

23. The method of claim 22, wherein

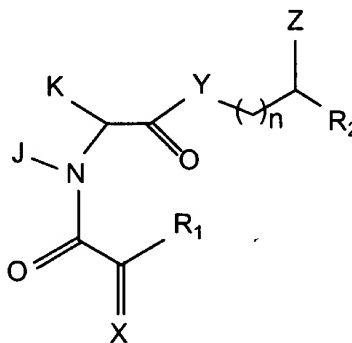
-if n is 0, X is O, Y is O, R<sub>1</sub> is 1,1-dimethyl-1-propyl, and R<sub>2</sub> is 2-phenylethyl, then Z is not 1,1-dimethyl-1-prop-2-enyl, phenyl, cyclohexyl, or 3-(N,N-diallyl)benzamide; and

-if n is 0, X is O, Y is O, R<sub>1</sub> is tert-butyl, and R<sub>2</sub> is 2-(3',4',5'-trimethoxyphenyl)ethyl, then <sup>D</sup>Z is not phenyl.

24. The method of claim 17, further comprising co-administering an effective amount of a neurotrophic factor to prevent neurodegeneration selected from the group consisting of nerve growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, and neurotrophin-3.

25. A method for promoting neuronal regeneration and growth in animals, comprising:

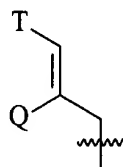
administering to said animal an effective amount of compound having an affinity for FKBP-type immunophilins according to formula I



Formula I

or a pharmaceutically acceptable salt thereof,

- wherein Y is CH<sub>2</sub>, O, NH, or N-(C1-C4 alkyl);
- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns, or



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- wherein Q is hydrogen, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl;
- wherein T is Ar or substituted 5-7 membered cycloalkyl with substituents at positions 3 and 4 which are independently selected from the group consisting of hydrogen, hydroxyl, O-(C1-C4)-alkyl or O-(C1-C4)-alkenyl and carbonyl;
- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl,

O-phenyl, amino, 1,2-methylenedioxy, carbonyl and phenyl;

- wherein  $R_1$  is either hydrogen or U; X is either oxygen or CH-U, provided that if  $R_1$  is hydrogen, then X is CH-U, or if X is oxygen then  $R_1$  is U;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar (Ar as described above);

- wherein J is hydrogen or C1 or C2 alkyl or benzyl; K is (C1-C4)-straight or branched alkyl, benzyl or cyclohexylethyl; or wherein J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain an oxygen (O), sulfur (S), SO or SO<sub>2</sub> substituted therein; and

- wherein n is 0-3.

26. The method of claim 25, further comprising co-administering an effective amount of a neurotrophic factor to promote neuronal regeneration selected from the group consisting of nerve growth factor, brain derived growth factor, glial derived growth factor, and neurotrophin-3.

27. The method of claim 25, wherein J and K are taken together to form a 5 membered heterocyclic ring.

28. The method of claim 27,

- wherein Z and  $R_2$  are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-

straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and

- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

29. The method of claim 28, wherein



- if X is O, Y is O, NH or N-(C1-C4 alkyl), R<sub>1</sub> is C1-C6 straight or branched alkyl, C2-C6 straight or branched alkenyl, C5-C7 cycloalkyl or cycloalkenyl substituted with C1-C4 straight or branched alkyl or C2-C4 straight or branched alkenyl, and Ar is 1-naphthyl, 2-naphthyl, indolyl, 2-furyl, 3-furyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl

- then (CH<sub>2</sub>)<sub>n</sub>Z and R<sub>2</sub> taken together do not form:

1) substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl

2) an alkyl or alkenyl chain with substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl

3) an alkyl or alkenyl chain substituted with C5-C7 cycloalkyl.

30. The method of claim 25, wherein J and K are taken together to form a 6 membered heterocyclic ring.

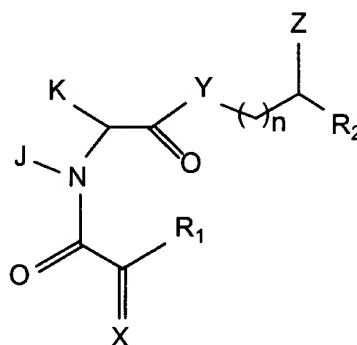
31. The method of claim 30,

- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and
- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

32. The method of claim 31, wherein
- if n is 0, X is O, Y is O, R<sub>1</sub> is 1,1-dimethyl-1-propyl, and R<sub>2</sub> is 2-phenylethyl, then Z is not 1,1-dimethyl-1-prop-2-enyl, phenyl, cyclohexyl, or 3-(N,N-diallyl)benzamide; and
  - if n is 0, X is O, Y is O, R<sub>1</sub> is tert-butyl, and R<sub>2</sub> is 2-(3',4',5'-trimethoxyphenyl)ethyl, then Z is not phenyl.
33. A method for stimulating the growth of damaged peripheral nerves, comprising:

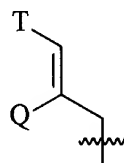
administering to said damaged peripheral nerves an effective amount of a compound having an affinity for FKBP-type immunophilins according to formula I



Formula I

or a pharmaceutically acceptable salt thereof,

- wherein Y is CH<sub>2</sub>, O, NH, or N-(C1-C4 alkyl);
- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns, or



- wherein Q is hydrogen, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl;
- wherein T is Ar or substituted 5-7 membered cycloalkyl with substituents at

positions 3 and 4 which are independently selected from the group consisting of hydrogen, hydroxyl, O-(C1-C4)-alkyl or O-(C1-C4)-alkenyl and carbonyl;

- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, 1,2-methylenedioxy, carbonyl and phenyl;

- wherein R<sub>1</sub> is either hydrogen or U; X is either oxygen or CH-U, provided that if R<sub>1</sub> is hydrogen, then X is CH-U, or if X is oxygen then R<sub>1</sub> is U;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar (Ar as described above);

- wherein J is hydrogen or C1 or C2 alkyl or benzyl; K is (C1-C4)-straight or branched alkyl, benzyl or cyclohexylethyl; or wherein J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain an oxygen (O), sulfur (S), SO or SO<sub>2</sub> substituted therein; and

- wherein n is 0-3.

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34. The method of claim 33, further comprising co-administering an effective amount of a neurotrophic factor to stimulate growth of the damaged peripheral nerve selected from the group consisting of nerve growth factor, brain derived growth factor, glial derived growth factor, and neurotrophin-3.

35. The method of claim 33, wherein J and K are taken together to form a 5 membered heterocyclic ring.

36. The method of claim 35,

- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and

- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which

may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

37. The method of claim 36, wherein

- if X is O, Y is O, NH or N-(C1-C4 alkyl), R<sub>1</sub> is C1-C6 straight or branched alkyl, C2-C6 straight or branched alkenyl, C5-C7 cycloalkyl or cycloalkenyl substituted with C1-C4 straight or branched alkyl or C2-C4 straight or branched alkenyl, and Ar is 1-naphthyl, 2-naphthyl, indolyl, 2-furyl, 3-furyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl

- then (CH<sub>2</sub>)<sub>n</sub>Z and R<sub>2</sub> taken together do not form:

- 1) substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl
- 2) an alkyl or alkenyl chain with substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl
- 3) an alkyl or alkenyl chain substituted with C5-C7 cycloalkyl.

38. The method of claim 33, wherein J and K are taken together to form a 6 membered heterocyclic ring.

39. The method of claim 38,

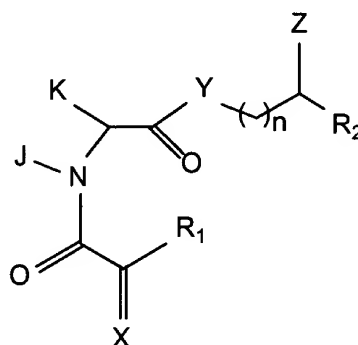
- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and

- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

40. The method of claim 39, wherein
- if n is 0, X is O, Y is O, R<sub>1</sub> is 1,1-dimethyl-1-propyl, and R<sub>2</sub> is 2-phenylethyl, then Z is not 1,1-dimethyl-1-prop-2-enyl, phenyl, cyclohexyl, or 3-(N,N-diallyl)benzamide; and
  - if n is 0, X is O, Y is O, R<sub>1</sub> is tert-butyl, and R<sub>2</sub> is 2-(3',4',5'-trimethoxyphenyl)ethyl, then Z is not phenyl.

41. A method for stimulating neurite outgrowth by a nerve cell, comprising:
- administering to said nerve cell an effective amount of compound having an affinity for FKBP-type immunophilins according to formula I



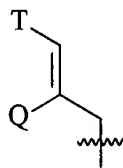
Formula I

or a pharmaceutically acceptable salt thereof,

- wherein Y is CH<sub>2</sub>, O, NH, or N-(C1-C4 alkyl);
- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2



heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns, or



- wherein Q is hydrogen, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl;
- wherein T is Ar or substituted 5-7 membered cycloalkyl with substituents at positions 3 and 4 which are independently selected from the group consisting of hydrogen, hydroxyl, O-(C1-C4)-alkyl or O-(C1-C4)-alkenyl and carbonyl;
- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, 1,2-methylenedioxy, carbonyl and phenyl;
- wherein R<sub>1</sub> is either hydrogen or U; X is either oxygen or CH-U, provided that if R<sub>1</sub> is hydrogen, then X is CH-U, or if X is oxygen then R<sub>1</sub> is U;
- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkyl, (C5-C7)-cycloalkenyl substituted

with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar (Ar as described above);

- wherein J is hydrogen or C1 or C2 alkyl or benzyl; K is (C1-C4)-straight or branched alkyl, benzyl or cyclohexylethyl; or wherein J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain an oxygen (O), sulfur (S), SO or SO<sub>2</sub> substituted therein; and

- wherein n is 0-3.

42. The method of claim 41, further comprising co-administering an effective amount of a neurotrophic factor to stimulating neurite outgrowth selected from the group consisting of nerve growth factor, brain derived growth factor, glial derived growth factor, and neurotrophin-3.

43. The method of claim 41, wherein J and K are taken together to form a 5 membered heterocyclic ring.

44. The method of claim 43,

- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;

- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and

- wherein Ar is selected from the group consisting of monocyclic and bicyclic heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

45. The method of claim 44, wherein

- if X is O, Y is O, NH or N-(C1-C4 alkyl), R<sub>1</sub> is C1-C6 straight or branched alkyl, C2-C6 straight or branched alkenyl, C5-C7 cycloalkyl or cycloalkenyl substituted with C1-C4 straight or branched alkyl or C2-C4 straight or branched alkenyl, and Ar is 1-naphthyl, 2-naphthyl, indolyl, 2-furyl, 3-furyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl

- then (CH<sub>2</sub>)<sub>n</sub>Z and R<sub>2</sub> taken together do not form:

- 1) substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl
- 2) an alkyl or alkenyl chain with substituted or unsubstituted indolyl, 2-furyl, 3-furyl, thiazolyl, 2-thienyl, 3, thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl
- 3) an alkyl or alkenyl chain substituted with C5-C7 cycloalkyl.

46. The method of claim 41, wherein J and K are taken together to form a 6 membered heterocyclic ring.

47. The method of claim 46,

- wherein Z and R<sub>2</sub> are independently Ar, (C5-C7)-cycloalkyl substituted (C1-C6)-straight or branched alkyl or alkenyl, (C5-C7)-cycloalkenyl substituted (C1-C6)-straight or branched alkyl or alkenyl, or Ar substituted (C1-C6)-straight or branched alkyl or alkenyl, wherein in each case, one or two carbon atoms of the straight or branched alkyl or alkenyl groups may be substituted with 1-2 heteroatoms selected from the group consisting of oxygen, sulfur, SO and SO<sub>2</sub> in chemically reasonable substitution patterns;
- wherein U is hydrogen, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, (C5-C7)-cycloalkenyl substituted with (C1-C4)-straight or branched alkyl or (C1-C4)-straight or branched alkenyl, [(C1-C4)-alkyl or (C1-C4)-alkenyl]-Ar or Ar; and
- wherein Ar is selected from the group consisting of monocyclic and bicyclic

heterocyclic aromatic ring systems with individual ring sizes being 5 or 6 which may contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halo, hydroxyl, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, (C1-C6)-straight or branched alkyl or (C1-C6)-straight or branched alkenyl, O-(C1-C4)-straight or branched alkyl or O-(C1-C4)-straight or branched alkenyl, O-benzyl, O-phenyl, amino, and 1,2-methylenedioxy.

48. The method of claim 47, wherein

-if n is 0, X is O, Y is O, R<sub>1</sub> is 1,1-dimethyl-1-propyl, and R<sub>2</sub> is 2-phenylethyl, then Z is not 1,1-dimethyl-1-prop-2-enyl, phenyl, cyclohexyl, or 3-(N,N-diallyl)benzamide; and

-if n is 0, X is O, Y is O, R<sub>1</sub> is tert-butyl, and R<sub>2</sub> is 2-(3',4',5'-trimethoxyphenyl)ethyl, then Z is not phenyl.